REMARKS

The Amendment, filed in response to the Office Action mailed October 5, 2009, is believed to be fully responsive to all issues raised in the Action. Favorable reconsideration on the merits and allowance of the application are respectfully requested.

Claims Disposition and Summary of Amendments

Claims 1-13 are all the claims pending in the application. Claims 11-13 are withdrawn from consideration as being drawn to non-elected invention. Claims 1-10 were considered and all stand rejected.

Applicant thanks the Examiner for entering the amendments presented on June 3, 2009.

Upon entry of the amendment, which is respectfully requested, claim 1 will be amended to more clearly set forth the feature of the claimed subject matter. Support for the amended claim can be found, for example, in paragraphs [0062] to [0065] of the specification as originally filed. Claims 3 and 10 are amended to correct a typographical error and use the language which are in conformity with the amended claim 1. No new matter is introduced.

Formal Matters

Applicant again notes that the Office Action Summary, boxes 4 and 6 incorrectly indicate claims 10-13 are withdrawn and claims 1-9 are considered. As the Detailed Action correctly indicates claims 1-10 are considered and claims 11-13 are withdrawn. A correct indication of claims disposition in a next Office Action is respectfully requested.

Response to Rejections under 35 U.S.C. § 103

1. Summary of Office Action

In the Office Action, claims 1-9 are rejected under 35 U.S.C. 103(a) as assertedly being unpatentable over Patel et al. (US Pre-Grant Publication 2003/0064097) ("Patel") in combination with Kawamura et al. (US Pre-Grant Publication 2004/0219208) ("Kawamura").

In the Office Action, claim 10 is rejected under 35 U.S.C. 103(a) as assertedly being unpatentable over the combined teachings of Patel and Kawamura as set forth above with respect to claim 1 in combination with Nielsen et al. (USPN 5,716,558) ("Nielsen").

The Examiner's characterization of the cited references and discussions of patentability are provided on pages 2-9 of the Office Action. The Examiner also provide kind comments on the Applicant's arguments, for which Applicant thank.

2. Applicant's Response

In response, without conceding the rejections, Applicant amends claim 1 in order to more clearly set forth the claimed subject matter.

In addition to the amendments made to claim 1, Applicant provides following arguments.

With respect to the Examiner's assertion that Applicants' argument that the references fail to show certain features of the subject invention is not persuasive, because the features upon which Applicants rely (i.e., crystallinity of paclitaxel) are not recited in the rejected claims, Applicant amends claim 1 to recite such feature. Amendment to claim 1 is made solely in order to advance the prosecution of the application.

One skilled in the art would not have been motivated to combine references

Applicant again respectfully submits that a person ordinary skilled in the art would not be motivated to combine Patel and Kawamura since their objects are clearly different from each other.

Specifically, the object of Patel is improving the solubility of hydrophobic active ingredients in order to improve delivery of the hydrophobic active ingredients, while Kawamura relates to releasing drugs in sustained manner. The increase in solubility of an active ingredient means that the active ingredient can dissolve into a biological fluid such as gastric juice better and faster, thereby increasing the bioavailability of the active ingredient in vivo. On the other hand, sustained release is a kind of time release technology employed in formulating a medicine in order to have a drug dissolve slowly and release a drug over time (*see* "http://en.wikipedia.org/wiki/ Sustained_release" ("in sustained release … formulated to dissolve slowly and release a drug over time").

No guidance to choose and combine paclitaxel and supercritical fluid process

In addition, the subject invention improves the solubility of, especially, paclitaxel, by using a supercritical fluid, thereby changing the crystallinity of paclitaxel. That is, the feature of the subject invention resides in the unique combination of a drug and a process for forming a solid dispersion thereof. Such inventive beneficial effects, *i.e.*, increased solubility of a paclitaxel solid dispersion, can be fully supported by the results of Test Example 1 (in particular, Table 25) of the specification as originally filed).

On the contrary, according to Patel, paclitaxel is embedded in a boilerplate list of pharmaceutically active ingredients, and there is no working example confirming an improved solubility of a composition comprising paclitaxel; and Kawamura only teaches that removal of water and organic solvent using supercritical fluid. Further, both of the cited references fail to disclose any relationship between solubility and crystallinity of a drug changed by using a supercritical fluid. Considering unpredictability in the art, therefore, one skilled in the art would not have reasonable expectation of success in reach the claimed invention.

Accordingly, even if they are combined together, a person skilled in the art would not have been able to select paclitaxel and supercritical fluid method and conceive the unique process for the improvement of paclitaxel solid dispersion of the subject invention.

(Response to Examiner's Comments)

Also, it is noted that the Examiner asserts "Concerning the unexpectedly remarkable effects achieved by the instant invention are also considered as being unpersuasive. Applicants draw a comparison to two specific Examples (Ex. 2 and 3) in attempt to demonstrate that the invention of Patel teaches away from the subject invention. The comparison is unpersuasive, first, because Applicants are relying on preferred teachings to teach away. To this, the Examiner respectively points out that "[t]he use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." Also, "[a] reference may be relied upon

for all that it would have reasonably suggested to one having ordinary skill in the art, including nonpreferred embodiments" (MPEP §2123)."

In response, while agreeing that a cited reference should be considered in its totality, Applicant respectfully traverses the Examiner's assertion. That is, regarding the cited portion of MPEP §2123, Applicant respectfully submits that the portion is related to standard for determining an anticipation under 35 U.S.C. § 102, rather than § 103. For anticipation determination, a single reference must teach all and every limitation of the claimed subject matter and the disclosure of the single reference must be considered regardless whether the disclosure is about preferred embodiment or disadvantageous comparative examples. However, in determining obviousness under 35 U.S.C. § 103, MPEP states "The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. *In re Hedges,* 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986) (Applicant's claimed process for sulfonating diphenyl sulfone at a temperature above 127°C was contrary to accepted wisdom because the prior art as a whole suggested using lower temperatures for optimum results as evidenced by charring, decomposition, or reduced yields at higher temperatures.). Furthermore, "[k]nown disadvantages in old devices which would naturally discourage search for new inventions may be taken into account in determining obviousness." *United States v. Adams,* 383 U.S. 39, 52, 148 USPQ 479, 484 (1966)." MPEP 2145. X.3. Emphasis added.

Claimed invention shows unexpectedly remarkable effects

Moreover, the effects stemming from the unique combination of paclitaxel and a supercritical fluid are recognized as unexpectedly remarkable compared with those of the cited reference. Specifically, the solubilities of paclitaxel solid dispersions prepared by the supercritical fluid process of the subject invention are remarkably higher (about 3,000 times) than that of the solid dispersion prepared by using liquid carbon dioxide or a conventional paclitaxel powder (see Table 25 of the subject specification). In contrast, although the compositions are not for paclitaxel, the dissolution ratios of the glyburide composition in Example 2 and the progestetone composition in Example 3 of Patel show merely 2 and 3 times higher than that of the pure bulk drug (see Figures 1, 2A and 2B of Patel). Furthermore, the amounts of surfactants (e.g., Myrj 52) comprised in the composition for further improving solubility of the subject invention, i.e., 2.5 to 25g, is much lower than those employed in Examples 2 to 5, and 13 to 28 of Patel.

Accordingly, the subject invention defined in claims 1 to 9 and claim 10 reciting claim 1 is evidently patentable and unobvious over the cited references. Withdrawal of the rejections is respectfully requested.

(Response to Examiner's Comments)

Applicant notes that the Examiner asserts that Applicant's argument of unexpected results is not persuasive, because Applicant argues the achievement of unexpected results over the teachings of Patel alone.

Applicant respectfully disagrees. According to MPEP 716.02(e),

> "Applicants may compare the claimed invention with prior art that is more closely related to the invention than the prior art relied upon by the examiner. *In re Holladay*, 584 F.2d 384, 199 USPQ 516 (CCPA 1978); *Ex parte Humber*, 217 USPQ 265 (Bd. App. 1961) (Claims to a 13-chloro substituted compound were rejected as obvious over nonchlorinated analogs of the claimed compound. Evidence showing unexpected results for the claimed compound as compared with the 9-, 12-, and 14- chloro derivatives of the compound rebutted the *prima facie* case of obviousness because the compounds compared against were closer to the claimed invention than the prior art relied upon.) Although evidence of unexpected results must compare the claimed invention with the closest prior art, applicant is not required to compare the claimed invention with subject matter that does not exist in the prior art. *In re Geiger*, 815 F.2d 686, 689, 2 USPQ2d 1276, 1279 (Fed. Cir. 1987) (Newman, J., concurring) (Evidence rebutted *prima facie* case by comparing claimed invention with the most relevant prior art. Note that the majority held the Office failed to establish a *prima facie* case of obviousness.); *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966) (Requiring applicant to compare claimed invention with polymer suggested by the combination of references relied upon in the rejection of the claimed invention under 35 U.S.C. 103 "would be requiring comparison of the results of the invention with the results of the invention." 357 F.2d at 422, 148 USPQ at 714.). "

Therefore, Applicant's comparison of the unexpected results shown in the specification with the embodiments of Patel, which is believed to be the closest prior art, are proper and should be fully considered.

For the reasons discussed above, Applicant believes the rejections are not sustainable and withdrawal of the rejections is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Sunhee Lee/

Sunhee Lee
Registration No. 53,892

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
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